

## **AMENDMENTS**

The Examiner is respectfully requested to make the following amendments.

### **IN THE CLAIMS:**

1. (Original) A method for making a prognosis of disease course in a human cancer patient, the method comprising the steps of:

- (a) obtaining a sample of a tumor from the human cancer patient;
- (b) determining a level of nuclear localization of p53 protein in the tumor sample and comparing the level of nuclear localization of p53 protein in the tumor sample with the level of nuclear localization of p53 protein in a non-invasive, non-metastatic tumor sample;
- (c) determining a level of thrombospondin 1 expression in the tumor sample and comparing the level of thrombospondin 1 expression in the tumor sample with the level of thrombospondin 1 expression in a non-invasive, non-metastatic tumor sample;
- (d) determining by immunohistochemistry an extent of microvascularization in the tumor sample and comparing the extent of microvascularization in the tumor sample with the extent of microvascularization in a non-invasive, non-metastatic tumor sample; and
- (e) preparing a prognostic index comprising the results of the determination of the levels of nuclear localization of p53, thrombospondin 1 expression, and the extent of microvascularization in the tumor sample,

wherein said prognosis is predicted from considering a likelihood of further neoplastic disease which is made when the level of nuclear localization of in the tumor sample is greater than the level of nuclear localization of p53 protein in the non-invasive, non-metastatic tumor sample; the level of thrombospondin 1 expression in the tumor sample is less than the level of thrombospondin 1 expression in the non-invasive, non-metastatic tumor sample; and the extent of microvascularization in the tumor sample is greater than the extent of microvascularization in the non-invasive, non-metastatic tumor sample.

2. (Original) The method of Claim 1, wherein the level of nuclear localization of p53 protein in the tumor sample is from about twofold to about tenfold greater than the level of nuclear localization of p53 protein in the non-invasive, non-metastatic tumor sample.

3. (Original) The method of Claim 1, wherein the level of thrombospondin 1 expression in the tumor sample is from about twofold to about tenfold less than the level of thrombospondin 1 expression in the non-invasive, non-metastatic tumor sample.

4. (Original) The method of Claim 1, wherein the extent of microvascularization in the tumor sample is from about twofold to about tenfold greater than the extent of microvascularization in the non-invasive, non-metastatic tumor sample.

5. (Original) The method of Claim 1, wherein the level of nuclear localization of p53 protein in the tumor sample is from about twofold to about tenfold greater than the level of nuclear localization of p53 protein in the non-invasive, non-metastatic tumor sample, and wherein the level of thrombospondin 1 expression in the tumor sample is from about twofold to about tenfold less than the level of thrombospondin 1 expression in the non-invasive, non-metastatic tumor sample and wherein the extent of microvascularization in the tumor sample is from about twofold to about tenfold greater than the extent of microvascularization in the non-invasive, non-metastatic tumor sample.

6. (Original) The method of Claim 1, wherein the level of nuclear localization of p53 protein in the tumor sample is from about fivefold greater than the level of nuclear localization of p53 protein in the non-invasive, non-metastatic tumor sample, and wherein the level of thrombospondin 1 expression in the tumor sample is from about fivefold less than the level of thrombospondin 1 expression in the non-invasive, non-metastatic tumor sample and wherein the extent of microvascularization in the tumor sample is from about sixfold greater than the extent of microvascularization in the non-invasive, non-metastatic tumor sample.

7. (Original) The method of Claim 1, wherein the level of nuclear localization of p53,

the level of thrombospondin 1 expression and the extent of microvascularization are determined by immunohistochemical staining.

8. (Original) The method of Claim 1 wherein the cancer is breast cancer.
9. (Original) The method of Claim 1 wherein the cancer is prostate cancer.
- 10 (Original) The method of Claim 1 wherein the cancer is melanoma.
- 11-20. (Withdrawn)